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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/771,312	JAKOBOVITS ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,14,15 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12, 14-15 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to the Amendment

The Amendment filed on 04/07/2006 in response to the previous Non-Final Office Action (1/13/2006) is acknowledged and has been entered.

12, 14-15 and 39 are currently pending and under consideration

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claims 12, 14-15 and 39 **remain** rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 12, 14-15 and 39 are directed to an isolated recombinant protein comprising the amino acid sequence of SEQ ID NO: 2, wherein the recombinant protein is encoded by a nucleotide sequence of SEQ ID NO: 1. However, neither the specification nor any art of record teaches what the amino acid sequence of SEQ ID NO: 2 is, how it functions, or a specific and well-established utility as claimed. The specification asserts (page 15, lines 28-29 and page 16, lines 1-18) that the polypeptides of the invention can be utilized to generate antibodies for use in detecting 84P2A9 overexpression or the metastasis of prostate cells and/or cells of other cancers expressing the gene. Thus, it presumed that there is a correlation between the overexpression of the polypeptide and a particular disease state. Furthermore, the specification teaches (page 18, lines 15-17) that the proteins of the invention may also be used in the forensic analysis of tissues of unknown origin.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended

definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where *specific* benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

Although the specification discloses a nexus between the polynucleotide expression and a disease state (see for example page 75, Example 3), the specification does not disclose a correlation between any specific disorder and an altered level or form of the claimed polypeptide. If a molecule such as the polypeptide of SEQ ID NO: 2 is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many polypeptides may be expressed in normal tissues, as well as diseased tissues. Therefore, one needs to know, e.g., that the claimed polypeptide is present only in cancer tissue to the exclusion of normal tissue. Thus, in the absence of any correlation between the claimed polypeptide with any known disease or disorder, any information obtained from various expression profiles in both normal and diseased tissue only serves as the basis for further research on the observation itself.

Furthermore, those of skill in the art recognize that over expression of a particular nucleic acid specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide expression. There are many steps in the pathway leading from DNA to protein, and all of them can, in principle, be regulated. For example, Alberts *et al.* (Molecular Biology of the Cell, 3rd edition, 1994, page 465) illustrate post-transcriptional regulation of ferritin wherein the translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferin receptor polypeptide is translated. Lewin, B. also teaches (Genes VI, Oxford University Press, Inc., NY, Chapter 29, 1997) that a major control point for genes exists during the initiation of transcription by the interaction of the RNA polymerase with its promoter. Concurring with Alberts *et al.*, Lewin

further acknowledges downstream control of gene expression since translation of mRNA in the cytoplasm is also a point of control. Also, with regards to tumor associated antigens, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Furthermore, Mallampalli *et al.* (Biochem. J. Vol. 318, 1996, pages 333-341) teach that the glucocorticoid, betamethasone, increased mRNA expression of cholinephosphate cytidylyltransferase (CT) as determined by RT-PCR and Southern analysis, but did not alter the levels of the CT enzyme as assayed by Western blotting (abstract, and page 339, 2nd column, 2nd paragraph). Finally, Lewin acknowledges that control of gene expression can occur at multiple stages and that production of RNA *cannot inevitably* be equated with production of protein. Thus, the predictability of protein translation and its possible utility as a diagnostic are not necessarily contingent on the levels of mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Therefore, absent evidence of the polypeptide expression including the correlation to a diseased state, one of skill in the art would not be able to predictably use the invention in a way that constitutes a specific and substantial utility and as disclosed do not meet the requirements of 35 U.S.C. §101 as being useful.

Claims 12, 14-15 and 39 also **remain** rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In response to the rejection, Applicants contend that while there are many other uses for the claimed polypeptide, for the purposes of prosecution, Applicants rely solely on the presently asserted utility of the claimed polypeptide as a target on cancerous prostate cells such that the alleged usefulness of the claimed subject matter as a diagnostic, noted by the Office in the last office action, is not relevant to the prosecution of the present case. Therefore, Applicants respectfully disagree with the Offices statements that the present specification has failed to disclose a correlation between a specific disorder and "an altered level or form of the claimed peptide". For example, Applicants assert that those of skill in the art recognize that the prostate is a gland which secretes a component of semen and that the prostate is a completely disposable organ evidenced by the common practice of surgically removing cancerous prostates from individuals diagnosed with

prostate cancer. In addition, Applicants submit that there are a number of art-recognized techniques that can be used to diagnose prostate cancer. Moreover, Applicants argue that there are a number of antibodies on the market that are used to treat cancer that cross react with normal tissue (i.e., Rituxan ® (Genetech) and Erbitux® (Imclone)). Accordingly, the commercial success of these antibodies demonstrates that this cross-reactivity is not alone sufficient to render such an antibody useless. As such, Applicants argue that one exemplary mechanism by which the present protein could find use is in the generation of antibodies that recognize the claimed protein that can be used alone or labeled with toxins, radioisotopes or other chemotherapeutic agents to inhibit the growth of prostate cancer cells expressing the claimed protein. Under this mechanism, Applicants assert that it is completely irrelevant whether normal, non-cancerous prostate cells express the claimed protein because the idea of the treatment is to kill as many cells as possible, wherein the presence of non-cancerous cells that express the claimed protein may actually potentiate the effectiveness of the labeled antibodies by bringing more of the label in proximity to cancer cells which are located near the non-cancerous cells. Applicants further submit that they have demonstrated in the specification that the claimed protein is expressed by cancerous prostate cancer cells in the form of mRNA expression, as well as in the Rule 1.132 declaration by Dr. Morrison provided with the last response. Applicants assert that Dr. Morrison's declaration also clearly demonstrates that antibodies which bind to the claimed protein are capable of binding prostate cancer cells which the Office admitted in the last Office Action. Accordingly, Applicants assert that the data and comments provided above clearly establish a link between the claimed protein and prostate cancer.

These arguments have been carefully considered, but are not found persuasive.

In the instant case, the Examiner recognizes that an Applicant may assert more than one practical application, but only one is necessary to satisfy the utility requirement. Thus, while the previous office action addressed one of the asserted utilities, i.e., diagnostic for prostate cancer, Applicant's appear to be arguing that the "one" asserted utility of the claimed polypeptide, for prosecution purposes, that satisfies the utility requirement is its usefulness as a target for cancerous prostate cancer cells. However, the Examiner does not see a difference in being a target for cancerous prostate cancer cells and being a diagnostic for prostate cancer cells. In other words, there still needs to be some type of expression pattern that would allow the claimed polypeptide to be useful as a "target" on prostate cancer cells vs. normal prostate cells and/or any other normal

tissue. Moreover, in response to Applicants assertion that that the claimed polypeptide is useful for generating antibodies against the claimed polypeptide and that antibody cross-reactivity, e.g., react with both cancer and normal tissues, is not alone sufficient to render such an antibody useless, as evidenced by the antibodies on the market (i.e., Rituxan ® (Genetech) and Erbitux® (Imclone)), the Examiner acknowledges and agrees with Applicants assertion that cross reactivity is not sufficient to render the antibody useless; and further, the Examiner appreciates Applicants for pointing out that there are many antibodies available on the market which show cross-reactivity to normal and cancerous tissues. However, the Examiner recognizes that the fact patterns involved between the commercially available antibodies and those which may be produced by the claimed polypeptide are different. For instance, the two commercially available antibodies referenced by Applicants have been individually taught in the prior art to be useful for inhibiting the development of cancer (package insert for Rituxan and Erbitux). As such, have utility for the treatment of cancer. In contrast, the specification does not appear to provide any objective evidence or guidance regarding the affects of an antibody alone or labeled with toxins radioisotopes or other chemotherapeutic agents generated by the claimed polypeptide for inhibiting the growth of prostate cancer cells expressing the claimed protein. In general, treatment of cancer is at most unpredictable as underscored by Gura (Science, v278, 1997, pp.1041-1042) who discusses the potential shortcomings of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice- particularly strains which have tumor suppressor gene knockouts, and problems of clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. Gura further teaches that very few drugs tested in xenografts models have made it to clinical practice and that attempts to use human cells in culture don't seem to be faring any better, partly because cell culture provides no information about whether a drug will make it to the tumor site (page 1041, 3rd paragraph). Lastly, the Examiner agrees with Applicants assertion that in the last Office Action the Examiner stated that Applicants have shown that the claimed protein can be detected on prostate cancer cells using immunohistochemistry. However, the Examiner, as stated in the prior office action, does not agree with the opinion that the level of

expression of 84P2A9 is higher in cancer tissue than in normal tissue because the declaration does not appear to suggest whether the protein is expressed in cancerous tissues to the exclusion of normal. Nor does the declaration nor specification appear to suggest any quantitative measurements. Thus, it is the Examiner opinion that the claimed polypeptide and antibodies generated by the claimed polypeptide are not supported by either a specific or substantial asserted utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-15 and 39 **remain** rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. THIS IS A BIOLOGICAL DEPOSIT REJECTION.

Because a microorganism is recited in the claims, it is essential to the invention recited in those claims. It must therefore be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the microorganism is not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the microorganism. The specification does not disclose a repeatable process to obtain the microorganism from a source, and it is not apparent if the microorganism is readily available to the public. It is noted that Applicants have deposited the organism under the requirements of the Budapest Treaty on January 6, 2000 with the American Type Culture Collection (ATCC), 1081 University Blvd. Manassas, VA 20110-2209 USA, and have identified it as ATCC Accession No. PTA-1151, but there is no indication in the specification as to public availability.

If the deposit was made under the terms of the Budapest Treaty, as it appears to have been from the enclosed Receipt from the ATCC, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the

specific strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

In response to this rejection, Applicants assert that the deposited material will remain deposited with the ATCC for 30 years from January, 2001 and will be publically available.

This statement has been carefully considered, but is not found persuasive.

In the instant case, the Examiner appreciates Applicants for attempting to overcome this rejection by asserting that the deposited material will remain deposited with the ATCC for 30 years from January, 2001 and will be publicly available. However, the Examiner recognizes that if the deposit was made under the terms of the Budapest Treaty, as it appears to have been from the enclosed Receipt from the ATCC, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that **the specific strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent**, would satisfy the deposit requirement made herein.

All other previous rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Conclusion

Therefore, No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

BF
6/15/2006